

REMARKS

The issues outstanding in the Office Action of August 4, 2009, are the rejections under 35 U.S.C. 102 and 103. Reconsideration of these issues, in view of the following discussion, is respectfully requested.

Rejection Under 35 U.S.C. 102

Claim 12 has been rejected under 35 U.S.C. 102 (b) over Login '237. Claim 12 has been canceled, and thus this rejection is moot. Withdrawal thereof is respectfully requested.

Rejection Under 35 U.S.C. 103

Claims 5 and 7-11 are rejected under 35 U.S.C. 103 over Login taken with Giberson and Boon. Reconsideration of this rejection is again respectfully requested.

Login discloses a process employing microwave irradiation along with a physiologic salt solution or a dilute aldehyde solution, to preserve tissue in the preparation of bioprosthesis for implantation into patient. In the method of Login et al., a specimen of biological tissue is immersed in an osmotically balanced solution (OBS). The purpose of utilizing OBS is to *prevent the loss* of important cellular constituents due to diffusion. See, col. 5, lines 9-11. This is consistent with "tissue fixing" e. g. by exposure to glutaraldehyde or formaldehyde, note the discussion of cell fixing at column 2, along 31-33 and lines 52-53 patent. Such "fixing" is *not* decellularization in a complete matter, so as remove all cells. Treatment or immersion a solution such as osmotically balanced solution does not enable removal of cellular components, even with the microwave radiation treatment of the patent. In Login's method, the tissue immersed in OBS initially at room temperature (approximately 20°C) is irradiated with microwave energy at a sufficient does and for a sufficient time such that the temperature of the solution is within the range of 35°C to 50°C. This time is short, e.g. between one and fifty seconds. See, e.g. claim 6. Thus, Login does not disclose a process which can result in complete decellularization.

In the present invention, the tissue immersed in the treating solution is irradiated with considerably greater intensity, e.g., with microwaves at a frequency of 2450MHz (the frequency

of a standard microwave oven) for a net period of time so as to achieve complete decellularization or for at least 1 hour while maintaining the temperature in the range of 0°C to 40°C, (see Claim 10). The duration of microwave irradiation in Claim 10 is at least 72 times greater than the duration of microwave irradiation of Login's method. Moreover, in Login, the microwave oven will be automatically shut off when the pre-set final irradiation temperature of the solution is obtained (col. 4, lines 65-67). In other words, Login never irradiates the tissue specimen in OBS with microwave energy at a dose and for a length of time such that temperature of the solution reaches above patentees' preset temperature of 35°C to 50°C. Such duration of microwave irradiation is not sufficient to achieve complete decellularization. With a large enough dose of microwave energy to remove cellular membrane and release intracellular components, such as in the present invention, it is necessary to cool the tissue in the treating solution to maintain the generating temperature from 0°C to 40°C as recited in the claims. Thus, the disclosure of Login is simply does not suggest to one of ordinary skill, particularly in the absence of a decellularizing chemical, complete decellularization and/or the conditions recited in the present invention. The osmotically balanced solutions (OBS) of Login et al. are free of any decellularizing chemical such as the presently recited detergents and, therefore, are not capable of decellularizing native biological tissues.

It is recognized that the Office Action uses the disclosures of Giberson and Boon to attempt to remedy the deficiencies of the primary reference. However, these secondary references fail to do so. In Giberson a tissue specimen is immersed in a formalin based solution, and irradiated with microwaves. Formalin is well known as a fixation chemical of biological tissues for microscopic inspection. Since the morphological characteristics of the tissue specimen must be preserved for diagnostic purposes, Giberson does not remove any cellular component from the tissue. Boon teaches the use of alcohol or glutaraldehyde as an immersion fluid (page 7, lines 51-55) when irradiating tissue with microwaves. Thus, again, only fixation is taught, and not complete decellularization. The secondary references accordingly do nothing to remedy the deficiencies of Login, and even in combination do not suggest the present claims. Accordingly, it is submitted that the rejection should be withdrawn.

It is anticipated that the next Office Action will resuscitate the prior rejection under 35 U.S.C. 112, arguing that the term "complete decellularization" lacks written description.

Applicants again strongly disagree. The specification states that the present methods result in decellularization “even in deep interior portions by irradiation with microwaves.” Moreover, paragraph 6 of the specification criticizes the prior art and teaches that because of prior art limitations, “complete decellularization and removal of bacteria and viruses are hardly possible for large tissue materials.” Later in the paragraph, it is further noted that known treating processes “do not assure complete inactivation of a viral contaminant and infection incidents may often occur from transplanted tissue...”. Paragraph 8 then indicates that it is an object of the invention to provide a method which can “eliminate or ameliorate disadvantages of the prior art, namely, a method which can accomplish, first, removal of cellular components.” Thus, it is submitted that the concept of “complete” decellularization is, in fact, taught, nearly in those words. Thus, the specification discusses “complete decellularization” as being necessary, and teaches that such is achieved the present method, see also page 12, paragraph 24 of the specification. It is well accepted that for written description, “ipsis verbis” support is not necessary. That is, the exact words recited in claims need not also be found in the specification, if the specific concept embodied in the words is taught to have invented by the inventors. See for example, *In re Wertheim et al.*, 541 F.2d257, 191 U.S.P.Q. 90 (CCPA 1976). Thus, the above noted discussion in the specification clearly teaches to one of ordinary skill in the art that the present invention involves “complete” decellularization, i.e., until no residual cell nuclei are observed on microscopic examination.

In conclusion, it is submitted that the claims are in condition for allowance, and passage to issue is respectfully requested. However, if the Examiner has any questions or comments, he or she is cordially invited to telephone the undersigned at the number below.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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